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SEARCH REQUEST FORM

Scientific and Technical Inf rmation Center

Requester's Full Name: Deborah A Davis Examiner #: 69897 Date: 11-22-02
Art Unit: 1641 Phone Number 308-4427 Serial Number: 09/889,520
Mail Box and Bldg/Room Location: 7D16 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Assay with reduced background

Inventors (please provide full names) Neil Lawrence and Matthew Wiatrowski

Earliest Priority Filing Date: 2-5-99

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

See attached Claims

Thank you

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Searcher: D. Schreiber
Searcher Phone #: 308-4279
Searcher Location: CM1 6A03
Date Searcher Picked Up:
Date Completed: 12/2/3
Searcher Prep & Review Time: 19
Clerical Prep Time:
Online Time: 47

Type of Search

NA Sequence (#)
AA Sequence (#)
Structure (#)
Bibliographic ✓
Litigation
Fulltext
Patent Family
Other

Vendors and cost where applicable

STN 138.34
Dialog
Questel/Orbit
Dr.Link
Lexis/Nexis
Sequence Systems
WWW/Internet
Other (specify)

PTO-1590 (8-01)

Davis 09/889,520

=> d his 1

(FILE 'HCAPLUS' ENTERED AT 08:32:40 ON 23 DEC 2002)
L18 1 DUP REM L16 L17 (0 DUPLICATES REMOVED)

=> d que l18
L1 212 SEA THERMOSTABLE(5A) KINASE#
L14 58 SEA RAVEN N?/AU
L15 66 SEA WICTOME M?/AU
L16 1 SEA L1 AND (L14 OR L15)
L17 0 SEA FILE=EMBASE L1 AND (L14 OR L15)
L18 1 DUP REM L16 L17 (0 DUPLICATES REMOVED)

Applicant 1

=> d ibib abs l18 1

L18 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:553690 HCAPLUS
DOCUMENT NUMBER: 133:161574
TITLE: Analyte assays with reduced background using **thermostable** reporter adenylate **kinase**
INVENTOR(S): **Raven, Neil David Hammond; Wictome, Matthew Patrick**
PATENT ASSIGNEE(S): Microbiological Research Authority, UK
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000046357	A1	20000810	WO 2000-GB315	20000203
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1151087	A1	20011107	EP 2000-901771	20000203
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002535985	T2	20021029	JP 2000-597417	20000203

PRIORITY APPLN. INFO.: GB 1999-2659 A 19990205
WO 2000-GB315 W 20000203

AB In an assay, an analyte is specifically assocd. with a reporter adenylate kinase, ADP is added and then formation of ATP is monitored. Prior to addn. of ADP, adenylate kinase other than reporter adenylate kinase is removed. Assay app. comprises a solid phase on which is immobilized the analyte or an antibody specific for the analyte, a reporter compn. comprising a **thermostable** adenylate **kinase** coupled to an antibody specific for the analyte, and ADP plus assocd. reagents for conversion of ADP into ATP by **thermostable** adenylate **kinase**. In particular, a rapid and sensitive method is provided for detection of the prion protein PrP (PrPC and PrPSc) in biol.

Search completed by David Schreiber 308-4292

materials.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Search completed by David Schreiber 308-4292

Davis 09/889,520

MODULATOR ON MG-2&, CA-2& **ATPASE** FROM NERVE-TISSUE
AUTHOR: MIKELADZE D G (Reprint)
CORPORATE SOURCE: ACAD SCI GESSR, INST PHYSIOL, TBILISI, GESSR (Reprint)
COUNTRY OF AUTHOR: GEORGIAN SOVIET SOCIALIST REPUBLIC
SOURCE: BIOCHEMISTRY-USSR, (1979) Vol. 44, No. 10, pp. 1469-1474.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 19

L13 ANSWER 30 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1968:401152 HCAPLUS
DOCUMENT NUMBER: 69:1152
TITLE: Properties of isoenzymes of adenosine triphosphate creatine phosphotransferase from rabbit muscles
AUTHOR(S): Dmitrenko, M. P.
CORPORATE SOURCE: Inst. Biochem., Kiev, USSR
SOURCE: Ukr. Biokhim. Zh. (1968), 40(1), 44-50
CODEN: UBZHAZ
DOCUMENT TYPE: Journal
LANGUAGE: Ukrainian

AB A study of the isoenzymic spectrum and properties of skeletal, cardiac, gastric, and uterine muscle creatine kinase was undertaken with grown rabbits. To sarcoplasmic proteins 0.5M Veronal-acetate buffer, pH 9, was added. The homogenates of these were centrifuged and the supernatants were used. The proteins were dialyzed prior to electrophoresis. The electrophoresis of the proteins was effected on a starch block with a AgCl electrode (Veronal-acetate buffer ionic strength 0.05, pH 9). The effect of temp. on isoenzymic activity was studied at 45.degree.. The effect of blood serum on creatine kinase activity was studied by the addn. of a soln. of the enzyme to the serum at a ratio of 4:1. The immunological properties of the isoenzyme were studied by use of purified skeletal creatine kinase as the antigen. The skeletal and cardiac muscles contained single isoenzymes which migrated to the cathode. The uterine tissues contained 1 isoenzyme which traveled to the anode. The gastric muscles contained 3 isoenzymes 1 of which migrated to the cathode and the other 2 to the anode. On the basis of the effect of temp. on enzymic activity the isoenzymes could be divided into 2 groups: **thermostable** consisting of the creatine **kinase** of the skeletal and cardiac muscles and isoenzymes II and III of the gastric muscles; thermolabile consisting of the creatine kinase of the uterine tissues and isoenzyme I of the gastric muscles. Blood serum depressed the activity of the isoenzymes but activated the purified creatine kinase of the uterus. Immunologically the **antibodies** in the blood serum inactivate the muscular isoenzymes. The isoenzymic spectrum during pregnancy is not changed. 20 references.

Search completed by David Schreiber 308-4292

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=> d his 1

(FILE 'MEDLINE, HCAPLUS, BIOSIS, SCISEARCH, EMBASE' ENTERED AT 08:22:12 ON 23 DEC 2002)

L13 30 DUP REM L11 L12 (20 DUPLICATES REMOVED)

=> d que l13

L1 212 SEA THERMOSTABLE(5A) KINASE#
L2 6 SEA L1 AND (IMMUNOGLOBULIN# OR ANTIBOD?)
L3 21 SEA L1 (5A)(DETECT? OR MEASUR? OR ANALY? OR ASSAY? OR QUANTIF? OR QUANTITA? OR TEST?)
L4 1 SEA L1 (5A) ADP (5A) ATP
L5 6 SEA L1 AND LUCIFERASE#
L6 6 SEA L1 AND ATPASE#
L7 1 SEA L1 AND CONJUGAT?
L8 45 SEA L1 AND (BACKGROUND OR INTERFERE? OR SPECIFIC?)
L9 15 SEA L8 AND (DETECT? OR MEASUR? OR ANALY? OR ASSAY? OR QUANTIF? OR QUANTITAT?)
L10 1 SEA L1 AND PRION#
L11 42 SEA (L2 OR L3 OR L4 OR L5 OR L6 OR L7) OR L9 OR L10
L12 8 SEA FILE=EMBASE (L2 OR L3 OR L4 OR L5 OR L6 OR L7) OR L9 OR L10
L13 30 DUP REM L11 L12 (20 DUPLICATES REMOVED)

=> d ibib abs l13 1-30

L13 ANSWER 1 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:78504 HCAPLUS
DOCUMENT NUMBER: 134:143870
TITLE: Thermostable nucleoside diphosphate kinase isoenzymes from Pyrococcus furiosus for nucleic acid detection
INVENTOR(S): Andrews, Christine Ann; Hartnett, James R.
PATENT ASSIGNEE(S): Promega Corporation, USA
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 15
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001007580	A1	20010201	WO 2000-US4206	20000218
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6235480	B1	20010522	US 1999-358972	19990721
EP 1198561	A1	20020424	EP 2000-919323	20000218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.:
US 1999-358972 A 19990721
US 1998-42287 A2 19980313
US 1999-252436 A2 19990218
WO 2000-US4206 W 20000218

Search completed by David Schreiber 308-4292

Davis 09/889,520

AB A thermostable nucleoside diphosphate kinase (NDPK) enzyme useful in a process for the detection of nucleic acid is disclosed. Cloning and expression of a gene encoding a long NDPK isoenzyme (NDPK-2) from thermophilic bacteria Pyrococcus furiosus is described. The nucleotide and encoded amino acid sequence of a N-terminal truncated isoenzyme of NDPK (NDPK-1) from P. furiosus is also disclosed. The enzyme, its variants and analogs exhibit higher NDPK activity at a temp. of about 50.degree. to about 90.degree. relative to NDPK activity at 37.degree.. Methods of obtaining, prepg. and using the enzyme are also disclosed.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

applicant

L13 ANSWER 2 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:553690 HCAPLUS
DOCUMENT NUMBER: 133:161574
TITLE: **Analyte assays** with reduced **background** using **thermostable** reporter adenylate **kinase**
INVENTOR(S): Raven, Neil David Hammond; Wictome, Matthew Patrick
PATENT ASSIGNEE(S): Microbiological Research Authority, UK
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000046357	A1	20000810	WO 2000-GB315	20000203
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1151087	A1	20011107	EP 2000-901771	20000203
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002535985	T2	20021029	JP 2000-597417	20000203

PRIORITY APPLN. INFO.: GB 1999-2659 A 19990205
WO 2000-GB315 W 20000203

AB In an **assay**, an **analyte** is **specifically** assocd. with a reporter adenylate kinase, ADP is added and then formation of ATP is monitored. Prior to addn. of ADP, adenylate kinase other than reporter adenylate kinase is removed. **Assay** app. comprises a solid phase on which is immobilized the **analyte** or an **antibody specific** for the **analyte**, a reporter compn. comprising a **thermostable** adenylate **kinase** coupled to an **antibody specific** for the **analyte**, and ADP plus assocd. reagents for conversion of **ADP** into **ATP** by **thermostable** adenylate **kinase**. In particular, a rapid and sensitive method is provided for **detection** of the **prion** protein PrP (PrPC and PrPSc) in biol. materials.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS

Search completed by David Schreiber 308-4292

ACCESSION NUMBER: 1996:694445 HCAPLUS
DOCUMENT NUMBER: 125:321325
TITLE: **Detection** and characterization of **thermostable** riboflavin **kinase** in the yeast Pichia guilliermondii
AUTHOR(S): Kashchenko, V. E.; Fayura, L. R.; Sibirnyi, A.A.
CORPORATE SOURCE: L'vov. Otd. regulyatornykh sistem Kletki, Lvov, 290005, Ukraine
SOURCE: Biokhimiya (Moscow) (1996), 61(9), 1589-1599
CODEN: BIOHAO; ISSN: 0320-9725
PUBLISHER: Nauka
DOCUMENT TYPE: Journal
LANGUAGE: Russian

AB Thermoinactivation of riboflavin kinase (I) was studied in cell-free exts. of p. guilliermondii; in this yeast, riboflavin phosphorylation is catalyzed by 2 enzymes, 1 of which is highly thermostable. The inactivation rate consts. (kin) at 90.degree. were 11.2 .times. 10-4 s-1 for one enzyme and 4.0 .times. 10-2 s-1 for the other enzyme. The I enzymes were not sepd. by (NH4)2SO4 fractionation of yeast proteins as well as by ion-exchange and gel permeation chromatogs. The enzymes were sepd. and purified by affinity chromatog. of cell-free yeast exts. on Blue Sepharose CL-6B and elution with ATP. The less-thermostable enzyme corresponded to a previously described I from P. guilliermondii, whereas the thermostable I was different in optimal pH and temp., had a higher activation energy of riboflavin phosphorylation, and very high affinities for riboflavin (Km = 0.65 .mu.M) and ATP (Km = 0.7 .mu.M).

L13 ANSWER 12 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2

ACCESSION NUMBER: 1997:122857 BIOSIS
DOCUMENT NUMBER: PREV199799429360
TITLE: **Detection** and characterization of **thermostable** riboflavin **kinase** in the yeast Pichia guilliermondii.
AUTHOR(S): Kashchenko, V. E. (1); Fayura, L. R.; Sibirnyi, A. A.
CORPORATE SOURCE: (1) Lvov Branch Cell Regulatory Systems, Palladin Inst. Biochemistry, Natl. Academy Sci. Ukraine, ul. Dragomanova 14/16, Lvov 290005 Ukraine
SOURCE: Biochemistry (Moscow), (1996) Vol. 61, No. 9, pp. 1125-1131.
ISSN: 0006-2979.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Thermal inactivation of riboflavin kinase (ATP: riboflavin-5'-phosphotransferase) in cell-free extract of the yeast P. guilliermondii revealed the existence of two enzymes catalyzing riboflavin phosphorylation in these cells. One is highly thermostable. The inactivation rate constants (k-in) for the enzymes at 90 degree C are 11.2-10-4 sec-1 and 4.0 cntdot 10-2 sec-1. The riboflavin kinases could not be separated by ammonium sulfate fractionation or by ion-exchange or gel permeation chromatographies of the yeast proteins. The enzymes were separated and purified using affinity chromatography of cell-free extracts on Blue Sepharose CL-6B by elution with ATP. The less thermostable-enzyme corresponds to the previously described riboflavin kinase from P. guilliermondii. The thermostable enzyme has distinct temperature and pH optima. It is also characterized by a higher activation energy for the riboflavin phosphorylation reaction and greater affinity to riboflavin (K-m = 0.65 mu-M) and ATP (K-m = 0.7 mu-M).

Search completed by David Schreiber 308-4292

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:185765 HCAPLUS
DOCUMENT NUMBER: 132:304843
TITLE: Building a thermostable membrane protein
AUTHOR(S): Zhou, Yufeng; Bowie, James U.
CORPORATE SOURCE: Department of Chemistry and Biochemistry, UCLA-DOE Laboratory of Structural Biology and Molecular Medicine, UCLA, Los Angeles, CA, 90095, USA
SOURCE: Journal of Biological Chemistry (2000), 275(10), 6975-6979
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The poor stability of membrane proteins in detergent soln. is one of the main tech. barriers to their structural and functional characterization. Here we describe a soln. to this problem for diacylglycerol kinase (DGK), an integral membrane protein from Escherichia coli. Twelve enhanced stability mutants of DGK were obtained using a simple screen. Four of the mutations were combined to create a quadruple mutant that had improved stability in a wide range of detergents. In n-octylglucoside, the wild-type DGK had a thermal inactivation half-life of 6 min at 55.degree., while the quadruple mutant displayed a half-life of 35 min at 80.degree.. In addn., the quadruple mutant had improved thermodn. stability. Our approach should be applicable to other membrane proteins that can be conveniently **assayed**.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000325755 EMBASE
TITLE: The 1.5 .ANG. resolution crystal structure of the carbamate kinase-like carbamoyl phosphate synthetase from the hyperthermophilic archaeon Pyrococcus furiosus, bound to ADP, confirms that this **thermostable** enzyme is a carbamate **kinase**, and a provides insight into substrate binding and stability in carbamate kinases.
AUTHOR: Ramon-Maiques S.; Marina A.; Uriarte M.; Fita I.; Rubio V.
CORPORATE SOURCE: V. Rubio, Instituto de Biomedicina de Valencia, Consejo Sup. Invest. Cie. (IBV-CSIC), C/Jaime Roig 11 46010, Valencia, Spain. rubio@ibv.csic.es
SOURCE: Journal of Molecular Biology, (2 Jun 2000) 299/2 (463-476). Refs: 39
ISSN: 0022-2836 CODEN: JMOBAK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Carbamoyl phosphate (CP), an essential precursor of arginine and the pyrirnidine bases, is synthesized by CP synthetase (CPS) in three steps. The last step, the phosphorylation of carbamate, is also catalyzed by carbamate kinase (CK), an enzyme used by microorganisms to produce ATP from ADP and CP. Although the recently determined structures of CPS and CK show no obvious mutual similarities, a CK-like CPS reported in hyperthermophilic archaea was postulated to be a missing link in the

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evolution of CP biosynthesis. The 1.5 .ANG. resolution structure of this enzyme from Pyrococcus furiosus shows both a subunit topology and a homodimeric molecular organization, with a 16-stranded open .beta.-sheet core surrounded by .alpha.-helices, similar to those in CK. However, the pyrococcal enzyme exhibits many solvent-accessible ion-pairs, an extensive, strongly hydrophobic, intersubunit surface, and presents a bound ADP molecule, which does not dissociate at 22.degree.C from the enzyme. The ADP nucleotide is sequestered in a ridge formed over. the C-edge of the core sheet, at the bottom of a large cavity, with the purine ring enclosed in a pocket **specific** for adenine. Overall, the enzyme structure is ill-suited for catalyzing the characteristic three-step reaction of CPS and supports the view that the CK-like CPS is in fact a highly thermostable and very slow (at 37.degree.C) CK that, in the extreme environment of P. furiosus, may have the new function of making, rather than using, CP. The thermostability of the enzyme may result from the extension of the hydrophobic intersubunit contacts and from the large number of exposed ion-pairs, some of which form ion-pair networks across several secondary structure elements in each enzyme subunit. The structure provides the first information on substrate binding and catalysis in CKs, and suggests that the slow rate at 37.degree.C is possibly a consequence of slow product dissociation. (C) 2000 Academic Press.

L13 ANSWER 5 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:299524 HCAPLUS
DOCUMENT NUMBER: 130:307540
TITLE: Production of the adenylate kinase free **luciferase** using recombinant Escherichia coli expression system
INVENTOR(S): Squirrell, David James; Price, Rachel Louise; Murphy, Melanie Jane
PATENT ASSIGNEE(S): The Secretary of State for Defence, UK
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9922004	A1	19990506	WO 1998-GB3034	19981009
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2307098	AA	19990506	CA 1998-2307098	19981009
AU 9893600	A1	19990517	AU 1998-93600	19981009
AU 731446	B2	20010329		
EP 1025235	A1	20000809	EP 1998-946599	19981009
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2001520888	T2	20011106	JP 2000-518095	19981009
US 2002045234	A1	20020418	US 2000-529722	20000419

PRIORITY APPLN. INFO.: GB 1997-22481 A 19971025
WO 1998-GB3034 W 19981009

AB Adenylate kinase contamination of **luciferase** can lead to

false-pos. signals when the enzyme is used anal. A method for producing **luciferase** which is substantially free of adenylate kinase is described. In this method substitution mutations were introduced into the E. coli adenylate kinase gene to generate a thermolabile kinase that was unstable at .gtoreq. 37.degree.. A plasmid bearing the gene for a thermostable **luciferase** was then introduced into this host such that the **luciferase** could be produced at a temp. that is permissive to the adenylate kinase. The culture then was raised to a higher temp. to denature the adenylate kinase which was present. The method can be generally applied to the prodn. of polypeptides free of specific contaminants.

recombinate

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:48100 HCAPLUS
DOCUMENT NUMBER: 130:150345
TITLE: Cloning and expression of thermostable glycerol kinase from Thermus flavus
INVENTOR(S): Nishiya, Yoshiaki; Kawamura, Yoshihisa; Yoshimoto, Tadashi
PATENT ASSIGNEE(S): Toyobo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11009279	A2	19990119	JP 1997-167265	19970624

product of kinase

AB The gene encoding a novel thermostable glycerol kinase is isolated from Thermus flavus strain TE4320 (DSM674). The enzyme exhibits a pH optimum 10.0, temp. optimum 65.degree., pI 4.3, Km 0.038 mM (glycerol), and mol. wt. 58,000 by SDS-PAGE or 220,000 by gel filtration. The gene may be used for the prodn. of the enzyme that is useful for the lipid and glycerol assay.

L13 ANSWER 7 OF 30 MEDLINE
ACCESSION NUMBER: 1999138212 MEDLINE
DOCUMENT NUMBER: 99138212 PubMed ID: 9972265
TITLE: A novel glycerol kinase from Flavobacterium meningosepticum: characterization, gene cloning and primary structure.
AUTHOR: Sakasegawa S; Yoshioka I; Koga S; Takahashi M; Matsumoto K; Misaki H; Ohshima T
CORPORATE SOURCE: Asahi Chemical Industry Co. Ltd., Shizuoka, Japan.. a9310932@ut.asahi-kasei.co.jp
SOURCE: BIOSCIENCE, BIOTECHNOLOGY, AND BIOCHEMISTRY, (1998 Dec) 62 (12) 2388-95.
Journal code: 9205717. ISSN: 0916-8451.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-E11880
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990324

Search completed by David Schreiber 308-4292

reagent was stable in soln. for .apprx.1 mo at 10.degree.. A method for simultaneously measuring the activities of PK and creatine kinase (CK) in a single specimen was also developed. This was based on the fact that the assay conditions for both enzymes were similar. This method was found to have a high degree of precision and a good correlation with resp. PK and CK assay methods. This simultaneous measurement may be useful for the accurate differential diagnosis of myocardial infarction.

L13 ANSWER 20 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 87128405 EMBASE
DOCUMENT NUMBER: 1987128405
TITLE: cAMP-associated inhibition of Na+-H+ exchanger in rabbit kidney brush-border membranes.
AUTHOR: Weinman E.J.; Shenolikar S.; Kahn A.M.
CORPORATE SOURCE: Division of Nephrology, Department of Internal Medicine, University of Texas Medical School, Houston, TX 77025, United States
SOURCE: American Journal of Physiology - Renal Fluid and Electrolyte Physiology, (1987) 252/1 (21/1) (F19-F25). CODEN: AJPFDM
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 002 Physiology
028 Urology and Nephrology
030 Pharmacology
029 Clinical Biochemistry
LANGUAGE: English
AB Adenosine 3',5'-cyclic monosphosphate (cAMP) inhibits the rate of bicarbonate reabsorption and the rate of Na+-H+ exchange transport in the apical membrane of the proximal convoluted tubule. To study the relation between cAMP, cAMP-dependent protein kinase, and Na+-H+ exchange transport, brush-border membrane vesicles from the rabbit kidney were phosphorylated in vitro. The rate of proton gradient-stimulated amiloride-inhibitable 22Na+ uptake was **measured** as an index of Na+-H+ exchange transport activity. The inclusion of cAMP (10-6 M) in a phosphorylating solution containing ATP decreased the 10-s uptake of amiloride-sensitive sodium from 2.25 .+-. 0.21 nmol/mg protein in controls to 1.94 .+-. 0.19 ($P < 0.001$). Incubation of vesicles in the presence of purified catalytic subunit of cAMP-dependent protein kinase inhibited the amiloride-sensitive uptake of 22Na+ at 10 s from 2.35 .+-. 0.49 nmol/mg protein to 2.05 .+-. 0.44 ($P < 0.005$). The inhibitory effect of both cAMP and catalytic subunit of cAMP-dependent protein **kinase** was blocked by the **specific thermostable** protein inhibitor of the **kinase**. These studies demonstrate that activation of endogenous membrane-bound cAMP-dependent protein kinase or exposure to exogenous catalytic subunit of cAMP-dependent protein kinase inhibits the rate of Na+-H+ exchange transport in the brush-border membrane of the rabbit kidney.

L13 ANSWER 21 OF 30 MEDLINE
ACCESSION NUMBER: 87125198 MEDLINE
DOCUMENT NUMBER: 87125198 PubMed ID: 3028154
TITLE: cAMP-associated inhibition of Na+-H+ exchanger in rabbit kidney brush-border membranes.
AUTHOR: Weinman E J; Shenolikar S; Kahn A M
SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY, (1987 Jan) 252 (1 Pt 2) F19-25.
Journal code: 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States

Search completed by David Schreiber 308-4292

Davis 09/889,520

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198703
ENTRY DATE: Entered STN: 19900303
Last Updated on STN: 19970203
Entered Medline: 19870302

AB Adenosine 3',5'-cyclic monophosphate (cAMP) inhibits the rate of bicarbonate reabsorption and the rate of Na+-H+ exchange transport in the apical membrane of the proximal convoluted tubule. To study the relation between cAMP, cAMP-dependent protein kinase, and Na+-H+ exchange transport, brush-border membrane vesicles from the rabbit kidney were phosphorylated in vitro. The rate of proton gradient-stimulated amiloride-inhibitable 22Na+ uptake was **measured** as an index of Na+-H+ exchange transport activity. The inclusion of cAMP (10(-6) M) in a phosphorylating solution containing ATP decreased the 10-s uptake of amiloride-sensitive sodium from 2.25 +/- 0.21 nmol/mg protein in controls to 1.94 +/- 0.19 (P less than 0.001). Incubation of vesicles in the presence of purified catalytic subunit of cAMP-dependent protein kinase inhibited the amiloride-sensitive uptake of 22Na+ at 10 s from 2.35 +/- 0.49 nmol/mg protein to 2.05 +/- 0.44 (P less than 0.005). The inhibitory effect of both cAMP and catalytic subunit of cAMP-dependent protein **kinase** was blocked by the **specific thermostable** protein inhibitor of the **kinase**. These studies demonstrate that activation of endogenous membrane-bound cAMP-dependent protein kinase or exposure to exogenous catalytic subunit of cAMP-dependent protein kinase inhibits the rate of Na+-H+ exchange transport in the brush-border membrane of the rabbit kidney.

L13 ANSWER 22 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:71027 HCAPLUS
DOCUMENT NUMBER: 108:71027
TITLE: Bacterial glucokinase as an enzymic reagent of good stability for measurement of creatine kinase activity
AUTHOR(S): Kondo, Hitoshi; Shiraishi, Takanari; Kageyama, Masao; Nagata, Kazuhiko; Tomita, Kosuke
CORPORATE SOURCE: Res. Dev. Cent., UNITIKA Ltd., Uji, 611, Japan
SOURCE: Journal of Clinical Biochemistry and Nutrition (1987), 3(1), 17-25
CODEN: JCBNER; ISSN: 0912-0009
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An enzymic reagent, that has long-term stability even in the liq. state, was successfully employed for the measurement of serum creatine kinase (CK) activity. The enzyme used was the thermostable glucokinase (GlcK) obtained from the thermophile Bacillus sterothermophilus. The reagent was stable in soln. for .apprx.1 mo at 6.degree. and for .apprx.1 wk at 30.degree.. This substitution of glucokinase for the hexokinase of the most commonly used hexokinase-glucose-6-phosphate dehydrogenase (HK-G6PDH) method results in a marked improvement of the method. The CK activity measured by the GlcK-G6PDH method was linear up to .apprx.2000 U/L at 37.degree.. The GlcK-G6PDH method gave satisfactory precision and reproducibility (coeff. of variation <2.17%). Over a wide range of CK activity, an excellent agreement was obtained between the GlcK-G6PDH and the HK-G6PDH methods.

L13 ANSWER 23 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1983:608829 HCAPLUS
DOCUMENT NUMBER: 99:208829

Search completed by David Schreiber 308-4292

ANSWER 1 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:875074 CAPLUS
DN 139:380024
TI Oligonucleotide probes and primers for diagnosing and monitoring autoimmune and chronic inflammatory diseases
IN Wohlgemuth, Jay; Fry, Kirk; Woodward, Robert; Ly, Ngoc
PA Expression Diagnostics, Inc., USA
SO PCT Int. Appl., 877 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003090694	A2	20031106	WO 2003-US13015	20030424
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004009479	A1	20040115	US 2002-131827	20020424
PRAI	US 2002-131827	A2	20020424		
	US 2001-296764P	P	20010608		
	US 2001-6290	A2	20011022		

AB Methods of diagnosing or monitoring auto immune and chronic inflammatory diseases, particularly systemic lupus erythematosus and rheumatoid arthritis, in a patient by detecting the expression level of one or more genes in a patient, are described. Oligonucleotide probes and primers for diagnosing or monitoring autoimmune and chronic inflammatory diseases, particularly systemic lupus erythematosus and rheumatoid arthritis and kits or systems contg. the same are also described. In one format, the gene expression system is immobilized on an array, e.g. a chip, plate, bead, pin, membrane, microfilter, oligonucleotide, cDNA, or polynucleotide microarray.

L6 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:377088 CAPLUS
DN 138:380384
TI Method and device for detecting and monitoring alcoholism and related diseases using microarrays
IN Harris, Adron; Mayfield, Dayne R.; Lewohl, Jo; Dodd, Peter R.
PA University of Texas System, USA
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003040414	A1	20030515	WO 2002-US35902	20021108
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,				

PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003104457 A1 20030605 US 2002-291247 20021107

PRAI US 2001-338270P P 20011108

AB A device and method for detecting, diagnosing, and or monitoring alcoholism and related disease states is disclosed. The device includes a substrate and one or more alcoholism-specific nucleic acids attached to the substrate. The substrate is contacted by a sample collected from a person with alcoholism or alc. abuse or an alc. related disease state, wherein contact occurs under pre-selected binding conditions that provides information that can be collected and recorded by a computer.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:521969 CAPLUS

DN 137:90000

TI Protein-protein interactions in adipocyte cells and method for selecting modulators of these interactions

IN Legrain, Pierre; Marullo, Stefano; Jockers, Ralf

PA Hybrigenics, Fr.; Centre National De La Recherche Scientifique

SO PCT Int. Appl., 125 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053726	A2	20020711	WO 2001-EP15423	20011228
WO 2002053726	A3	20030313		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003040089 A1 20030227 US 2002-38010 20020102

PRAI US 2001-259377P P 20010102

AB The present invention relates to protein-protein interactions of adipocyte. More specifically, the present invention relates to complexes of polypeptides, or polynucleotides encoding the polypeptides, fragments of the polypeptides, antibodies to the complexes. Selected Interacting Domains (SID) which are identified due to the protein-protein interactions, methods for screening drugs for agents which modulate the interaction of proteins, and pharmaceutical compns. that are capable of modulating the protein-protein interactions are further disclosed.

L6 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:978584 CAPLUS

DN 138:34125

TI Determining changes in phenotype-specific gene expression in a cell by measuring changes in housekeeping and phenotype-specific gene expression

IN Nishimura, Ichiro; Iida, Keisuke

PA USA

SO U.S. Pat. Appl. Publ., 21 pp.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI US 2002197640 A1 20021226 US 2002-174658 20020619
WO 2004000867 A1 20031231 WO 2002-US19705 20020731
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI US 2001-299910P P 20010621
US 2002-174658 A 20020619
AB The present invention provides an improved method for assessing, monitoring and/or detg. the phenotype of cells and tissues. One aspect of the present invention is a method of fabricating phenotype specific gene (PSGs) and house keeping gene (HKGs) targets onto a microarray. Another aspect of the present invention provides a compn. contg. PSGs and HKGs as targets for high throughput assays including microarray analyses. Another aspect of the present invention is accessing, monitoring and/or detg. the phenotype of tissue engineered cells derived from stem cells including embryonic stem cells, embryonic germ cells, fetal stem cells and adult stem cells by hybridizing cDNA probes to either PSG or HKG targets. These methods employ at least 25 PSG targets and no greater than 5000 HKG targets. Specific genes for use in measuring changes in given tissues are claimed.

L6 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:937303 CAPLUS
DN 138:20443
TI Endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes
IN Kondo, Akihiro; Takeda, Takeshi; Mizutani, Shigetoshi; Tsujimoto, Yoshimasa; Takashima, Ryokichi; Enoki, Yuki; Kato, Ikunoshin
PA Takara Bio Inc., Japan
SO Jpn. Kokai Tokkyo Koho, 386 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2002355079	A2	20021210	JP 2002-69354	20020313
PRAI JP 2001-73183	A	20010314		
JP 2001-74993	A	20010315		
JP 2001-102519	A	20010330		

AB A method and kit for detecting endocrine-disrupting chems. using DNA microarrays are claimed. The method comprises prepg. a nucleic acid sample contg. mRNAs or cDNAs originating in cells, tissues, or organisms which have been brought into contact with a sample contg. the endocrine disruptor. The nucleic acid sample is hybridized with DNA microarrays having genes affected by the endocrine disruptor or DNA fragments originating in these genes have been fixed. The results obtained are then compared with the results obtained with the control sample to select the gene affected by the endocrine disruptor. Genes whose expression is altered by tri-Bu tin, 4-octaphenol, 4-nonylphenol, di-N-Bu phthalate, dichlorohexyl phthalate, octachlorostyrene, benzophenone, diethylhexyl phthalate, diethylstilbestrol (DES), and 17-.beta. estradiol (E2), were found in mice by DNA chip anal.

L6 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:396056 CAPLUS

DN 137:119829
TI Gene expression profiling of testosterone and estradiol-17.beta.-induced prostatic dysplasia in noble rats and response to the antiestrogen ICI 182,780
AU Thompson, Christopher J.; Tam, Neville N. C.; Joyce, Jennifer M.; Leav, Irwin; Ho, Shuk-Mei
CS Department of Surgery-Division of Urology, University of Massachusetts Medical School, Worcester, MA, 01655, USA
SO Endocrinology (2002), 143(6), 2093-2105
CODEN: ENDOAO; ISSN: 0013-7227
PB Endocrine Society
DT Journal
LA English
AB We previously demonstrated that (1) treatment of Noble rats for 16 wk with testosterone (T) and estradiol-17.beta. (E2) led to 100% incidence of dorsolateral prostate (DLP) dysplasia and hyperprolactinemia and (2) blockade of PRL release with bromocriptine cotreatment significantly lowered the incidence of DLP dysplasia. In the current study, we sought to det. whether E2 exerts direct effects, independent of PRL, in this model system. The pure antiestrogen ICI 182,780 (ICI), reported to have no effect on PRL release in female rats, was administered biweekly to T + E2-treated rats at 3 mg/kg. ICI cotreatment completely prevented DLP dysplasia development but it also blocked hyperprolactinemia in the dual hormone-treated rats. Gene profiling with an 1185 gene rat cDNA array identified .apprxeq.100 genes displaying .gtoreq.3-fold changes in rat lateral prostates (LPs) following T + E2 treatment. Significantly more genes were up-regulated (77) than down-regulated (14), reflecting cellular/mol. changes assocd. with enhanced cell proliferation, DNA damage, heightened protein and RNA synthesis, increased energy metab., and activation of several proto-oncogenes and intracellular signaling pathways. Post hoc analyses, using quant. real-time RT-PCR, corroborated differential expression of eight genes, exhibiting three different patterns of altered expression. Genes encoding the early growth response protein 1 and metalloendopeptidase meprin .beta.-subunit were similarly altered in T + E2- and T + E2 + ICI-treated animals when compared with untreated controls. In contrast, transcripts of fos-related antigen-2, growth arrest and DNA damage-inducible protein-45, and signal transducer and activator of transcription-3 were significantly increased in the LPs of T + E2-treated animals, but the increases were reversed by cotreatment with ICI. Differential expression of fos-related antigen-2 and growth arrest and DNA damage-inducible protein-45 were further confirmed at the protein level by immunohistochem. Lastly, levels of A-RAF, VIP-1 receptor, and calpastatin mRNA were distinctly lessen in rat LPs under T + E2 influence, but rebound with ICI cotreatment. In conclusion, our findings further implicated pituitary PRL in the induction of dysplasia in rat LP. Gene profiling provided clues that mol. events related to enhancement of cell proliferation, DNA damage, and activation of protooncogenes and transforming factors may be causally linked to the genesis of LP dysplasia in this rat model.
RE.CNT 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:214668 CAPLUS
DN 137:150359
TI Identification of genes regulated by dexamethasone in multiple myeloma cells using oligonucleotide arrays
AU Chauhan, Dharminder; Auclair, Daniel; Robinson, Elisabeth K.; Hideshima, Teru; Li, Guilan; Podar, Klaus; Gupta, Deepak; Richardson, Paul; Schlossman, Robert L.; Krett, Nancy; Chen, Lan Bo; Munshi, Nikhil C.; Anderson, Kenneth C.
CS The Jerome Lipper Multiple Myeloma Center, Department of Adult Oncology, Dana Farber Cancer Institute, Harvard Medical School, Boston, MA, 02115, USA

SO Oncogene (2002), 21(9), 1346-1358
CODEN: ONCNES; ISSN: 0950-9232
PB Nature Publishing Group
DT Journal
LA English
AB Our previous studies have characterized Dexamethasone (Dex)-induced apoptotic signaling pathways in multiple myeloma (MM) cells; however, related transcriptional events are not fully defined. In the present study, gene expression profiles of Dex-treated MM cells were detd. using oligonucleotide arrays. Dex triggers early transient induction of many genes involved in cell defense/repair-machinery. This is followed by induction of genes known to mediate cell death and repression of growth/survival-related genes. The mol. and genetic alterations assocd. with Dex **resistance** in MM cells are also unknown. We compared the gene expression profiles of Dex-sensitive and Dex-resistant MM cells and identified a no. of genes which may confer Dex-**resistance**. Finally, gene profiling of freshly isolated MM patient cells validates our in vitro MM cell line data, confirming an in vivo relevance of these studies. Collectively, these findings provide insights into the basic mechanisms of Dex activity against MM, as well as mechanisms of Dex-**resistance** in MM cells. These studies may therefore allow improved therapeutic uses of Dex, based upon targeting genes that regulate MM cell growth and survival.
RE.CNT 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 25 MEDLINE on STN DUPLICATE 1
AN 2002345604 MEDLINE
DN 22081872 PubMed ID: 12087068
TI Critical involvement of p38 MAP **kinase** in pertussis toxin-induced cytoskeletal reorganization and lung permeability.
AU Garcia Joe G N; Wang Peiyi; Schaphorst Kane L; Becker Patrice M; Borbiev Talaibek; Liu Feng; Birukova Anna; Jacobs Keri; Bogatcheva Natalia; Verin Alexander D
CS Division of Pulmonary and Critical Care Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.. drgarcia@jhmi.edu
NC HL 03666 (NHLBI)
HL 58064 (NHLBI)
HL 60628 (NHLBI)
SO FASEB JOURNAL, (2002 Jul) 16 (9) 1064-76.
Journal code: 8804484. ISSN: 1530-6860.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200207
ED Entered STN: 20020629
Last Updated on STN: 20021218
Entered Medline: 20020723
AB Bordetella pertussis is an important cause of infection in humans worldwide, with full expression of the syndrome associated with characteristic increases in lung permeability and airway edema. The exact cellular mechanisms by which pertussis toxin (PTX) exerts pulmonary toxicity remain unknown, but may involve its ability to **ADP** -ribosylate-specific G-proteins. We determined that PTX directly and reproducibly reduced lung endothelial and epithelial cell barrier function in vitro and in vivo assessed by decreases in transmonolayer electrical **resistance** (TER) and isolated perfused lung preparations. Alterations in lung permeability began approximately 30 min after PTX and were dependent on intrinsic **ADP**-ribosyltransferase activity, as neither the cell binding beta-oligomer subunit or a genetically engineered PTX mutant (devoid of **ADP**-ribosyltransferase activity) altered TER. PTX-induced barrier dysfunction was associated with mild increases in F-actin stress fiber formation and causally linked to p38 MAP

kinase activities. PTX-mediated p38 MAP **kinase** activation did not involve either p42/p44 ERK, p60src, Rho family of GTPases, or phosphatidylinositol-3' **kinase** pathways. PTX-mediated decreases in TER were temporally linked to phosphorylation of the actin binding proteins Hsp27 and caldesmon, known substrates for the Ser/Thr **kinase** MAPKAP2, whose activity is regulated by p38 MAP **kinase**. In addition to defining novel signaling pathways involved in PTX-induced respiratory pathophysiology, these data suggest that the direct cell-activating effects of PTX be carefully considered as a potential limitation to its use as a tool in signal transduction analysis.

L6 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:649057 CAPLUS
DN 137:334408
TI Protein **kinase** C .epsilon. signaling complexes include metabolism- and transcription/translation-related proteins: complimentary separation techniques with LC/MS/MS
AU Edmondson, Ricky D.; Vondriska, Thomas M.; Biederman, Kelli J.; Zhang, Jun; Jones, Richard C.; Zheng, Yuting; Allen, David L.; Xiu, Joanne X.; Cardwell, Ernest M.; Pisano, Michael R.; Ping, Peipei
CS Proteomic Research Services, Inc., Ann Arbor, MI, 48108, USA
SO Molecular and Cellular Proteomics (2002), 1(6), 421-433
CODEN: MCPOBS; ISSN: 1535-9476
PB American Society for Biochemistry and Molecular Biology, Inc.
DT Journal
LA English
AB The serine/threonine **kinase** protein **kinase** C .epsilon. (PKC.epsilon.) has been shown to be a crit. component in the heart's **resistance** to cell death following ischemic insult. Recent studies have indicated that PKC.epsilon. forms multi-protein signaling complexes to accomplish signal transduction in cardiac protection. Using two-dimensional electrophoresis (2DE), combined with matrix-assisted laser desorption ionization mass spectrometry (MS), the initial anal. of these complexes identified signaling mols., structural proteins, and stress-activated proteins. The initial anal., although fruitful, was limited by the no. of proteins revealed on the 2D gels. It was also apparent that many known cardiac protective functions of PKC.epsilon. could not be fully accounted for by the proteins identified in the initial anal. Here we report the identification of an addnl. 57 proteins in PKC.epsilon. complexes using complimentary sepn. techniques, combined with high sensitivity MS. These techniques include 2DE or large format 1D SDS-PAGE followed by LC/MS/MS and soln. trypsin digestion followed by LC/MS/MS, all of which yielded novel data regarding PKC.epsilon. protein complexes. Nanoscale LC/MS/MS for the anal. of gel-isolated proteins was performed with sub-femtomole sensitivity. In contrast to 2DE analyses, the identification of proteins from 1D gels was independent of their visualization via staining and allowed for the identification of proteins with high isoelec. points. We found that PKC.epsilon. complexes contain numerous structural and signaling mols. that had escaped detection by our previous analyses. Most importantly, we identified two new groups of proteins that were previously unrecognized as components of the PKC.epsilon. complex: metab.-related proteins and transcription/translation-related proteins.
RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:763235 CAPLUS
DN 135:314399
TI Detection of variations in the DNA methylation profile of genes in the determining the risk of disease
IN Berlin, Kurt; Piepenbrock, Christian; Olek, Alexander
PA Epigenomics A.-G., Germany
SO PCT Int. Appl., 636 pp.

CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 68

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001077373	A2	20011018	WO 2001-DE1486	20010406
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	DE 10019058	A1	20011220	DE 2000-10019058	20000406
	WO 2001077373	A2	20011018	WO 2001-XA1486	20010406
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, CF, CG, CI, CM, GA, GW, ML, MR, NE, SN, TD, TG				
	WO 2001077373	A2	20011018	WO 2001-XB1486	20010406
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, CF, CG, CI, CM, GA, GW, ML, MR, NE, SN, TD, TG				
	EP 1274865	A2	20030115	EP 2001-953936	20010406
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	EP 1278892	A1	20030129	EP 2001-940158	20010406
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003531589	T2	20031028	JP 2001-575634	20010406
	EP 1360319	A2	20031112	EP 2001-955278	20010406
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003162194	A1	20030828	US 2003-240452	20030414
	JP 2004008217	A2	20040115	JP 2003-160375	20030605
PRAI	DE 2000-10019058	A	20000406		
	DE 2000-10019173	A	20000407		
	DE 2000-10032529	A	20000630		
	DE 2000-10043826	A	20000901		
	WO 2001-DE1486	W	20010406		
	WO 2001-EP3969	W	20010406		
	WO 2001-EP4016	W	20010406		
	EP 2002-90203	A	20020605		

AB The invention relates to an oligonucleotide kit as probe for the detection of relevant variations in the DNA methylation of a target group of genes. The invention further relates to the use of the same for detg. the gene variant with regard to DNA methylation, a medical device, using an oligonucleotide kit, a method for detg. the methylation state of an individual and a method for the establishment of a model for establishing the probability of onset of a disease state in an individual. Such

diseases may be: undesired pharmaceutical side-effects; cancerous diseases; CNS dysfunctions, injuries or diseases; aggressive symptoms or relational disturbances; clin., psychol. and social consequences of brain injury; psychotic disorders and personality disorders; dementia and/or assocd. syndromes; cardiovascular disease, dysfunction and damage; dysfunction, damage or disease of the gastrointestinal tract; dysfunction, damage or disease of the respiratory system; injury, inflammation, infection, immunity and/or anastasis; dysfunction, damage or disease of the body as an abnormal development process; dysfunction, damage or disease of the skin, muscle, connective tissue or bones; endocrine and metabolic dysfunction, damage or disease; headaches or sexual dysfunction. This abstr. record is one of several records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.

L6 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:338762 CAPLUS
DN 134:362292
TI Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
IN Farr, Spencer
PA Phase-1 Molecular Toxicology, USA
SO PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001032928	A2	20010510	WO 2000-US30474	20001103
	WO 2001032928	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-165398P P 19991105
US 2000-196571P P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to det. the hypersensitivity of individuals to a given agent, such as drug or other chem., in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes assocd. with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes assocd. with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes assocd. with hypersensitivity. The expression of the genes predetd. to be assocd. with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and app. useful for identifying hypersensitivity in a subject are also disclosed.

L6 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:411495 CAPLUS

DN 135:179631
TI Profiling changes in gene expression during differentiation and maturation of monocyte-derived dendritic cells using both oligonucleotide microarrays and proteomics
AU Le Naour, Francois; Hohenkirk, Lyndon; Grolleau, Annabelle; Misek, David E.; Lescure, Pascal; Geiger, James D.; Hanash, Samir; Beretta, Laura
CS Department of Microbiology and Immunology, University of Michigan, Ann Arbor, MI, 48109-0666, USA
SO Journal of Biological Chemistry (2001), 276(21), 17920-17931
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Dendritic cells (DCs) are antigen-presenting cells that play a major role in initiating primary immune responses. The authors have utilized two independent approaches, DNA microarrays and proteomics, to analyze the expression profile of human CD14+ blood monocytes and their derived DCs. Anal. of gene expression changes at the RNA level using oligonucleotide microarrays complementary to 6300 human genes showed that .apprx.40% of the genes were expressed in DCs. A total of 255 genes (4%) were regulated during DC differentiation or maturation. Most of these genes were not previously assocd. with DCs and included genes encoding secreted proteins as well as genes involved in cell adhesion, signaling, and lipid metab. Protein anal. of the same cell populations was done using two-dimensional gel electrophoresis. A total of 900 distinct protein spots were included, and 4% of them exhibited quant. changes during DC differentiation and maturation. Differentially expressed proteins were identified by mass spectrometry and found to represent proteins with Ca2+ binding, fatty acid binding, or chaperone activities as well as proteins involved in cell motility. In addn., proteomic anal. provided an assessment of post-translational modifications. The chaperone protein, calreticulin, was found to undergo cleavage, yielding a novel form. The combined oligonucleotide microarray and proteomic approaches have uncovered novel genes assocd. with DC differentiation and maturation and has allowed anal. of post-translational modifications of specific proteins as part of these processes.
RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:312014 CAPLUS
DN 136:64938
TI Toward elucidating the global gene expression patterns of developing Arabidopsis: parallel analysis of 8 300 genes by a high-density oligonucleotide probe array
AU Zhu, Tong; Budworth, Paul; Han, Bin; Brown, Devon; Chang, Hur-Song; Zou, Guangzhou; Wang, Xun
CS Torrey Mesa Research Institute, Inc., San Diego, CA, 92121, USA
SO Plant Physiology and Biochemistry (Paris, France) (2001), 39(3-4), 221-242
CODEN: PPBIEX; ISSN: 0981-9428
PB Editions Scientifiques et Medicales Elsevier
DT Journal
LA English
AB Arabidopsis thaliana has been widely used as a model system, in various aspects of biol. studies, such as genomics, genetics, cellular, developmental and mol. biol. In order to reveal the mol. events and regulatory networks controlling Arabidopsis development and responses to genetic and environmental changes, we designed and used a high-d. oligonucleotide probe array (GeneChip) to profile global gene expression patterns. The Arabidopsis oligonucleotide probe array consists of probes from 8 300 unique Arabidopsis genes, which covers approx. one-third of the genome. Global transcription profiles of A. thaliana in various developmental stages, and their responses to different environments were generated using this microarray, and archived. Here, we analyze data sets

derived from nineteen independent expts. Constitutively and differentially expressed genes in seedlings, roots, leaves, inflorescences, flowers and siliques at different developmental stages were identified. Functions of these genes based on homologs were detd. and categorized. Our results provide insight into the coordinated transcriptional regulation of the genes during plant growth and development.

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 25 MEDLINE on STN DUPLICATE 2
AN 2000204406 MEDLINE
DN 20204406 PubMed ID: 10739474
TI Inorganic polyphosphate and polyphosphate **kinase**: their novel biological functions and applications.
AU Shiba T; Tsutsumi K; Ishige K; Noguchi T
CS Division of Molecular Chemistry, Graduate School of Engineering, Hokkaido University, Sapporo, 060-8628, Japan.. shiba@dove-mc.eng.hokudai.ac.jp
SO BIOCHEMISTRY, (2000 Mar) 65 (3) 315-23. Ref: 36
Journal code: 0376536. ISSN: 0006-2979.
CY RUSSIA: Russian Federation
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200007
ED Entered STN: 20000720
Last Updated on STN: 20000720
Entered Medline: 20000712
AB In this review, we discuss the following two subjects: 1) the physiological function of polyphosphate (poly(P)) as a regulatory factor for gene expression in Escherichia coli, and 2) novel functions of E. coli polyphosphate **kinase** (PPK) and their applications. With regard to the first subject, it has been shown that E. coli cells in which yeast exopolyphosphatase (poly(P)ase), PPX1, was overproduced reduced **resistance** to H2O2 and **heat** shock as did a mutant whose polyphosphate **kinase** gene is disrupted. Sensitivity to H2O2 and **heat** shock evinced by cells that overproduce PPX1 is attributed to depressed levels of rpoS expression. Since rpoS is a central element in a regulatory network that governs the expression of stationary-phase-induced genes, poly(P) affects the expression of many genes through controlling rpoS expression. Furthermore, poly(P) is also involved in expression of other stress-inducible genes that are not directly regulated by rpoS. The second subject includes the application of novel functions of PPK for nucleoside triphosphate (NTP) regeneration. Recently E. coli PPK has been found to catalyze the kination of not only **ADP** but also other nucleoside diphosphates using poly(P) as a phospho-donor, yielding NTPs. This nucleoside diphosphate **kinase**-like activity of PPK was confirmed to be available for NTP regeneration essential for enzymatic oligosaccharide synthesis using the sugar nucleotide cycling method. PPK has also been found to express a poly(P):AMP phosphotransferase activity by coupling with adenylate **kinase** (ADK) in E. coli. The ATP-regeneration system consisting of ADK, PPK, and poly(P) was shown to be promising for practical utilization of poly(P) as ATP substitute.

L6 ANSWER 15 OF 25 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2001:301446 BIOSIS
DN PREV200100301446
TI Complement-mediated effect of rituximab in B-cell lymphoproliferative disorders involves caspase-independent signaling pathways and correlates with CD20 expression.
AU Bellosillo, B. [Reprint author]; Villamor, N. [Reprint author]; Colomer, D. [Reprint author]; Marce, S. [Reprint author]; Esteve, J. [Reprint

author]; Campo, E. [Reprint author]; Lopez-Guillermo, A. [Reprint author]; Montserrat, E. [Reprint author]

CS Unitat d'Hematopatologia, Servei d'Hematologia, IDIBAPS, Hospital Clinic, Barcelona, Spain

SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 305a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)

LA English

ED Entered STN: 27 Jun 2001
Last Updated on STN: 19 Feb 2002

AB Rituximab is a monoclonal antibody directed against the CD20 antigen, which is restricted to normal and malignant B cells. The mechanism of action of Rituximab includes complement-mediated and antibody-dependent cellular cytotoxicity, as well as apoptosis induction. We have analyzed the in vitro effect of Rituximab in cells from 41 patients with B-cell lymphoproliferative disorders (23 CLL, 15 MCL, 2 FL and 1 HCL). Flow cytometry (FC) was used to assess cell viability by analyzing annexin V binding and to quantify CD20, CD55 and CD59 expression. Cells were incubated overnight with 50mug/ml Rituximab in the presence or absence of 10% human AB serum. Rituximab produced no effect when used alone, but induced complement-dependent cell death (CDC) in 7/23 CLL, 15/15 MCL, 2/2 FL and 1/1 HCL. This effect was completely abolished by **heat** -inactivation of human AB serum. Rituximab-induced CDC was only observed in those patients with more than 50.000 CD20 molecules/cell. Pre-incubation with anti-CD59 increased the cytotoxic effect of Rituximab. Moreover, in non-responders anti-CD59 overcame the **resistance** to Rituximab. The study of the signaling pathways involved in Rituximab-induced CDC showed neither cleavage of poly-**ADP** ribose polymerase nor activation of caspase-3. In addition, no cells with a hypodiploid DNA content were detected, and Rituximab-induced CDC was not prevented by the caspase-inhibitor N-benzyloxycarbonyl-Val-Ala-Asp-fluromethyl ketone (ZVAD.fmk), with this suggesting a caspase-independent mechanism. Pre-incubation of cells with PP2, a Src-family **kinase** inhibitor, did not modify the Rituximab-induced CDC. Incubation with Rituximab in the presence of AB serum was followed by a decrease in the mitochondrial transmembrane potential (DELTAPSIm) and a generation of reactive oxygen species (ROS) as assessed by FC. Rituximab-induced CDC was blocked by the pre-incubation of cells with N-acetyl-L-cysteine or Tiron, two ROS scavengers, indicating that the cytotoxic effect was due to the generation of O2 radicals. In conclusion, our results suggest that CD20, CD59 and complement play a role in the cytotoxic effect of Rituximab, with this being mediated by a caspase-independent process that involves ROS generation and loss of mitochondrial potential.

L6 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:795994 CAPLUS

DN 132:31744

TI Gene probes used for genetic profiling in healthcare screening and planning

IN Roberts, Gareth Wyn

PA Genostic Pharma Ltd., UK

SO PCT Int. Appl., 745 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9964627	A2	19991216	WO 1999-GB1780	19990604

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,
JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,
MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,
MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI GB 1998-12099 A 19980606
GB 1998-13291 A 19980620
GB 1998-13611 A 19980624
GB 1998-13835 A 19980627
GB 1998-14110 A 19980701
GB 1998-14580 A 19980707
GB 1998-15438 A 19980716
GB 1998-15574 A 19980718
GB 1998-15576 A 19980718
GB 1998-16085 A 19980724
GB 1998-16086 A 19980724
GB 1998-16921 A 19980805
GB 1998-17097 A 19980807
GB 1998-17200 A 19980808
GB 1998-17632 A 19980814
GB 1998-17943 A 19980819

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies which comprises of the identification of the core group of genes and their sequence variants required to provide a broad base of clin. prognostic information - "genostics". The "Genostic" profiling of patients and persons will radically enhance the ability of clinicians, healthcare professionals and other parties to plan and manage healthcare provision and the targeting of appropriate healthcare resources to those deemed most in need. The use of this invention could also lead to a host of new applications for such profiling technologies, such as identification of persons with particular work or environment related risk, selection of applicants for employment, training or specific opportunities or for the enhancing of the planning and organization of health services, education services and social services.

L6 ANSWER 17 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:795993 CAPLUS
DN 132:31743
TI Gene probes used for genetic profiling in healthcare screening and planning
IN Roberts, Gareth Wyn
PA Genostic Pharma Limited, UK
SO PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DT Patent

LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9964626	A2	19991216	WO 1999-GB1779	19990604
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2330929	AA	19991216	CA 1999-2330929	19990604
	AU 9941586	A1	19991230	AU 1999-41586	19990604
	AU 766544	B2	20031016		
	AU 9941587	A1	19991230	AU 1999-41587	19990604
	GB 2339200	A1	20000119	GB 1999-12914	19990604
	GB 2339200	B2	20010912		
	EP 1084273	A1	20010321	EP 1999-925207	19990604
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2003528564	T2	20030930	JP 2000-553616	19990604
	US 2003198970	A1	20031023	US 2002-206568	20020729
PRAI	GB 1998-12098	A	19980606		
	GB 1998-28289	A	19981223		
	GB 1998-16086	A	19980724		
	GB 1998-16921	A	19980805		
	GB 1998-17097	A	19980807		
	GB 1998-17200	A	19980808		
	GB 1998-17632	A	19980814		
	GB 1998-17943	A	19980819		
	US 1999-325123	B1	19990603		
	WO 1999-GB1779	W	19990604		

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies.

L6 ANSWER 18 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:736897 CAPLUS
DN 131:347500
TI Expression of transgenes in plants using promoter and terminator sequences from Coix
IN Kriz, Alan L.; Luethy, Michael H.; Voyles, Dale A.
PA Dekalb Genetics Corporation, USA
SO PCT Int. Appl., 240 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9958659	A2	19991118	WO 1999-US10776	19990514
	WO 9958659	A3	20000120		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6635806	B1	20031021	US 1998-78972	19980514
	CA 2328129	AA	19991118	CA 1999-2328129	19990514
	AU 9939957	A1	19991129	AU 1999-39957	19990514
	EP 1076706	A2	20010221	EP 1999-923112	19990514
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	BR 9910455	A	20011127	BR 1999-10455	19990514
	JP 2002533057	T2	20021008	JP 2000-548450	19990514
	ZA 2000006576	A	20020213	ZA 2000-6576	20001113
PRAI	US 1998-78972	A1	19980514		
	WO 1999-US10776	W	19990514		

AB Methods and compns. for the expression of transgenes in monocot plants including maize are disclosed. In the invention, gene silencing is avoided by use of monocot-homeologous sequences from plants of the genus Coix for transformation. Included in these transgene sequences are Coix promoters, enhancers, coding sequences and terminators. Suitable alternatives to maize-derived transgenes are desirable for expression in maize in that homol.-based gene silencing can limit or effectively eliminate transgene expression.

L6 ANSWER 19 OF 25 MEDLINE on STN DUPLICATE 3
AN 1998307958 MEDLINE
DN 98307958 PubMed ID: 9642282
TI **Heat** shock protein 72 modulates pathways of stress-induced apoptosis.
AU Buzzard K A; Giaccia A J; Killender M; Anderson R L
CS Trescowthick Research Laboratories, Peter MacCallum Cancer Institute, St. Andrews Place, East Melbourne, Victoria, Australia, 3002.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Jul 3) 273 (27) 17147-53. Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199808
ED Entered STN: 19980817
Last Updated on STN: 19980817
Entered Medline: 19980806
AB The **resistance** to stress-induced apoptosis conferred by the thermotolerant state or by exogenous expression of HSP72 was measured in mouse embryo fibroblasts. The induction of thermotolerance protects cells from **heat**, tumor necrosis factor alpha (TNFalpha), and ceramide-induced apoptosis but not from ionizing radiation. Because the development of thermotolerance is associated with increased levels of **heat** shock proteins, we determined whether constitutive expression of one of the major inducible **heat** shock proteins, HSP72, could also protect cells from stress-induced apoptosis. Cells expressing constitutive HSP72 were shown to have significantly reduced levels of apoptosis after **heat**, TNFalpha, and ceramide but not after ionizing radiation. Activation of stress-activated protein **kinase**

/c-Jun N-terminal **kinase** (SAPK/JNK) was found to be strongly inhibited in thermotolerant cells after **heat** shock but not after other stresses. Cells that constitutively express HSP72 did not demonstrate decreased SAPK/JNK activation after any of these stresses. Thus, factors other than HSP72 that are induced in the thermotolerant state are able to reduce activation of SAPK/JNK after **heat** stress. Notably, the level of activation of SAPK/JNK did not correlate with the amount of apoptosis detected after different stresses. Constitutive HSP72 expression inhibited poly(**ADP**-ribose) polymerase cleavage in cells after **heat** shock and TNFalpha but not after ceramide or ionizing radiation. The results suggest either that SAPK/JNK activation is not required for apoptosis in mouse embryo fibroblasts or that HSP72 acts downstream of SAPK/JNK. Furthermore, the data support the concept that caspase activity, which can be down-regulated by HSP72, is a crucial step in stress-induced apoptosis. Based on data presented here and elsewhere, we propose that the **heat** shock protein family can be classified as a class of anti-apoptotic genes, in addition to the Bcl-2 and inhibitor of apoptosis protein families of genes.

L6 ANSWER 20 OF 25 MEDLINE on STN DUPLICATE 4
AN 97415610 MEDLINE
DN 97415610 PubMed ID: 9271409
TI Role of the human **heat** shock protein hsp70 in protection against stress-induced apoptosis.
AU Mosser D D; Caron A W; Bourget L; Denis-Larose C; Massie B
CS Biotechnology Research Institute, National Research Council of Canada, Montreal, Quebec.. dick.mosser@nrc.ca
SO MOLECULAR AND CELLULAR BIOLOGY, (1997 Sep) 17 (9) 5317-27.
Journal code: 8109087. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199709
ED Entered STN: 19971008
Last Updated on STN: 20000303
Entered Medline: 19970922
AB **Resistance** to stress-induced apoptosis was examined in cells in which the expression of hsp70 was either constitutively elevated or inducible by a tetracycline-regulated transactivator. **Heat**-induced apoptosis was blocked in hsp70-expressing cells, and this was associated with reduced cleavage of the common death substrate protein poly(**ADP**-ribose) polymerase (PARP). **Heat**-induced cell death was correlated with the activation of the stress-activated protein **kinase** SAPK/JNK (c-Jun N-terminal **kinase**). Activation of SAPK/JNK was strongly inhibited in cells in which hsp70 was induced to a high level, indicating that hsp70 is able to block apoptosis by inhibiting signaling events upstream of SAPK/JNK activation. In contrast, SAPK/JNK activation was not inhibited by **heat** shock in cells with constitutively elevated levels of hsp70. Cells that constitutively overexpress hsp70 resist apoptosis induced by ceramide, a lipid signaling molecule that is generated by apoptosis-inducing treatments and is linked to SAPK/JNK activation. Similar to **heat** stress, **resistance** to ceramide-induced apoptosis occurs in spite of strong SAPK/JNK activation. Therefore, hsp70 is also able to inhibit apoptosis at some point downstream of SAPK/JNK activation. Since PARP cleavage is prevented in both cell lines, these results suggest that hsp70 is able to prevent the effector steps of apoptotic cell death. Processing of the CED-3-related protease caspase-3 (CPP32/Yama/apopain) is inhibited in hsp70-expressing cells; however, the activity of the mature enzyme is not affected by hsp70 in vitro. Caspase processing may represent a critical **heat**-sensitive target leading to cell death that is inhibited by the chaperoning function of hsp70. The inhibition of SAPK/JNK signaling

and apoptotic protease effector steps by hsp70 likely contributes to the **resistance** to stress-induced apoptosis seen in transiently induced thermotolerance.

L6 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:584258 CAPLUS
DN 127:259159
TI Identifying the major proteome components of Haemophilus influenzae type-strain NCTC 8143
AU Link, Andrew J.; Hays, Lara G.; Carmack, Edwin B.; Yates, John R., III
CS Dep. Molecular Biotechnology, Washington Univ., Seattle, WA, 98195, USA
SO Electrophoresis (1997), 18(8), 1314-1334
CODEN: ELCTDN; ISSN: 0173-0835
PB Wiley-VCH
DT Journal
LA English
AB With the completion of the H. influenzae Rd genomic sequence, the identity is known of most of the theor. proteins in the proteome of this bacterium. However, the most abundant components of the actual proteome are unknown. Using mass spectrometry and 2-dimensional gel electrophoresis (2-DE), the most abundant proteins were sequenced and analyzed obsd. in the ATCC ref. strain of H. influenzae, NCTC 8143 (303 of 400 Coomassie-stained 2-DE spots). To automate the identification of 2-DE spots, a liq. autosampler was coupled to a microcolumn liq. chromatog. electrospray ionization tandem mass spectrometer capable of identifying 22 spots per day. From the 303 sequenced spots, 263 unique proteins were identified . Most of the abundant proteins lie in an isoelec. point range of pH 4-7 and a mol. mass range of 10-100 kDa. Of the obsd. proteins, the most abundant is the outer membrane protein P2. Based on variety and abundance, proteins involved in energy metab. and macromol. synthesis are the dominant classes of proteins. Unexpectedly, tryptophanase was identified as a highly abundant protein in the strain NCTC 8143 whose sequence is not present in the genome of the Rd strain. By searching the tandem mass spectra against the translated genomic sequence, several proteins were identified which were not annotated in the genomic sequence. Surprisingly, 22% of the identified 2-DE spots represent isoforms in which gene products with the same primary sequence have different obsd. pI and Mr, indicating that these proteins are post-translationally processed. Although most proteins' predicted and obsd. isoelec. points and mol. masses show reasonable concordance, the obsd. values for several proteins deviate from the predicted values. These anomalies may represent either highly processed proteins or misinterpretations of the genomic sequence. Using the technol. developed in this project, the protein expression of other strains of H. influenzae grown under different environmental conditions can be compared to identify differences in their proteomes.

L6 ANSWER 22 OF 25 MEDLINE on STN DUPLICATE 5
AN 94165003 MEDLINE
DN 94165003 PubMed ID: 8119977
TI Genetically altered levels of inorganic polyphosphate in Escherichia coli.
AU Crooke E; Akiyama M; Rao N N; Kornberg A
CS Department of Biochemistry, Stanford University School of Medicine, California 94305.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 Mar 4) 269 (9) 6290-5.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199404
ED Entered STN: 19940412
Last Updated on STN: 19970203
Entered Medline: 19940404
AB The ppk gene encoding polyphosphate **kinase** (PPK), the enzyme in

Escherichia coli that makes long chains of polyphosphate (polyP) reversibly from ATP, was disrupted by insertion of a kanamycin **resistance** gene. Expression of the exopolyphosphatase gene (ppx) immediately downstream of ppk in the operon was likewise disrupted. Cells were also transformed with a high-copy-number plasmid bearing ppk. Genetically altered polyP levels were estimated in cell extracts by the PPK conversion of **ADP** to ATP. PolyP levels (microgram/10(11) cells) near 2.0 were reduced in the ppk(-)-ppx- mutants to 0.16 and increased more than 100-fold (e.g. 220) in cells transformed with multiple copies of ppk. Mutant cells, lacking the long polyP chains, showed a growth lag following dilution of a stationary-phase culture. PolyP-deficient cells exhibit a striking phenotype in their failure to survive in stationary phase and loss of **resistance** to **heat** (55 degrees C) and to oxidants (42 mM H2O2). High polyP levels are also associated with reduced survival.

L6 ANSWER 23 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:20120 CAPLUS
DN 114:20120
TI Investigation of the properties of bovine heart creatine **kinase** cross-linked with dimethyl suberimidate
AU Sheehan, Helen; O'Kennedy, Richard; Kilty, Cormae
CS Sch. Biol. Sci., Dublin City Univ., Dublin, Ire.
SO Biochimica et Biophysica Acta (1990), 1041(2), 141-5
CODEN: BBACAQ; ISSN: 0006-3002
DT Journal
LA English
AB Dimeric bovine heart creatine **kinase** (EC 2.7.3.2) has been cross-linked with the bifunctional reagent di-Me suberimidate at several concns. to yield modified enzyme with enhanced stability towards **heat** denaturation. The degree of thermal stability is dependant on the degree of crosslinking with optimal stabilization occurring when .apprx.1/2 of all the available amino groups are covalently attached to di-Me suberimidate. Accelerated storage studies were performed and the results used to predict the storage time of the native and modified enzyme at lower temps. The cross-linked deriv. was predicted to have a longer shelf-life at 4.degree. than the native enzyme. Modification caused a redn. in the specific activity of the enzyme. The pH profile was altered following crosslinking, but the Km's were not changed. The modified enzyme exhibited a marked **resistance** to the action of some denaturing agents.

L6 ANSWER 24 OF 25 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1983:199073 BIOSIS
DN PREV198375049073; BA75:49073
TI PYRUVATE **KINASE** EC-2.7.1.40 CONGENITAL HEMOLYTIC ANEMIA EVIDENCE OF DOUBLE HETERO ZYGOSITY AND LACK OF ENZYME COOPERATIVITY.
AU SCHROETER W [Reprint author]; SCHARNETZKY M L M; TILLMAN W; WINKLER H
CS DEP PAEDIATR, UNIV GOETTINGEN, FED REP GER
SO Human Genetics, (1982) Vol. 60, No. 4, pp. 381-386.
CODEN: HUGEDQ. ISSN: 0340-6717.
DT Article
FS BA
LA ENGLISH
AB Double heterozygosity of pyruvate **kinase** (PK) deficiency associated with hereditary hemolytic anemia is emphasized by studies of a kindred harboring 2 distinct mutant forms of this enzyme. The hematologically unaffected parents exhibit slightly reduced PK activity, a normal Hill coefficient and a normal thermodynamic dissociation constant for the overall reaction. The paternal enzyme is characterized by normal substrate affinities and decreased activities with the substrate analogs CDP and GDP, whereas the maternal enzyme shows normal affinity for PEP [phosphoenolpyruvate], but an increased affinity for **ADP** and low thermostability. The erythrocytes of the parents apparently contain a